SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Internal (Acute) Electrical Cardioversion Defibrillation System
Device Trade Name:	ALERT® System (ALERT® Companion™ with Software version V1.08, ALERT® Catheter, and ALERT® Interface Cable)
Applicant's Name:	EP MedSystems, Inc. Cooper Run Executive Park 575 Route 73 N., Unit D West Berlin, NJ 08091-9293
Premarket Approval Application (PMA) Number:	P990069
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	November 27, 2002

II. INDICATIONS FOR USE

The ALERT® System is indicated for use in patients who are candidates for transvenous electrical cardioversion for the treatment of atrial fibrillation.

III. CONTRAINDICATIONS

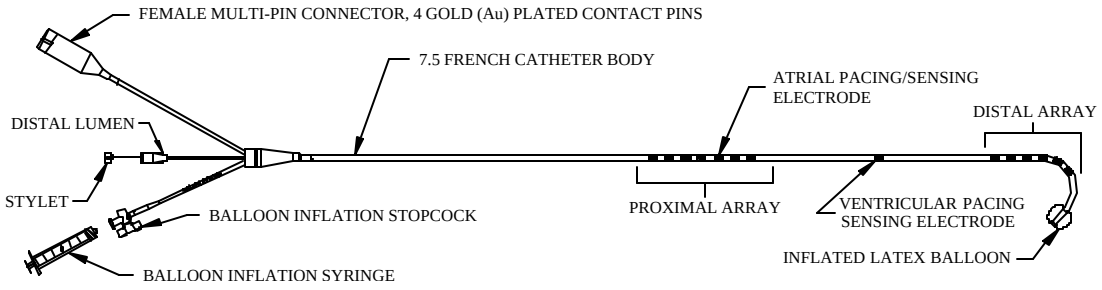
The **ALERT®** System is contraindicated when any of the following conditions exist:

- The patient is not a suitable candidate for the placement and use of temporary intracardiac pacing leads,
- The patient is not a suitable candidate for internal atrial cardioversion,
- The patient has had a peripheral embolism or stroke within three months of the proposed date of cardioversion,
- The patient has a mechanical tricuspid or pulmonary valve (a prosthetic tissue valve is permissible), or
- The patient has a heart condition for which defibrillation is contraindicated.

IV. DEVICE DESCRIPTION

The EP MedSystems, Inc. **A**trial **L**ow **E**nergy **R**eversion **T**herapy (ALERT®) System is comprised of the ALERT® Catheter, the ALERT® Companion, and the ALERT® Interface Cable that connects the two units. The ALERT® Catheter is an atrial defibrillation catheter with sensing, pacing and pressure measurement capabilities. The catheter interfaces with the ALERT® Companion, which is a software-controlled ECG monitor/recorder and defibrillator.

A. ALERT® Catheter (Fig. 1)



The ALERT® Catheter is a flow-directed, balloon-tipped atrial defibrillation catheter (Fig. 1)with additional atrial and ventricular sensing, single channel switchable atrial or ventricular bradycardia pacing, and pressure measurement capabilities. It has a nominal usable length of 110 ± 5 cm. The catheter body consists of radiopaque polyurethane 7.5 French, multi-lumen tubing. One 0.028 inch diameter distal lumen centered in the tubing is circumscribed by six smaller lumens.

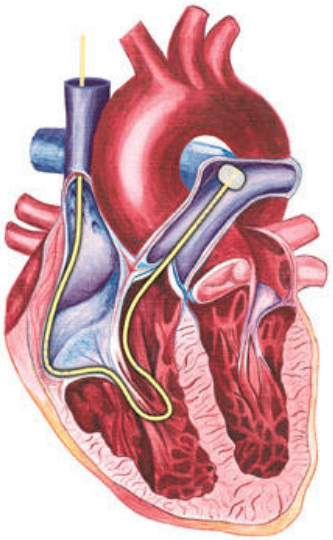


Fig. 2

This center lumen facilitates the passage of a standard 0.021 inch guidewire to ease catheter insertion (Fig. 2) and may also be used for blood sampling, drug infusion, and/or pressure measurements (Right Atrium, Right Ventricle, Pulmonary Capillary Wedge Pressure, Mean Pulmonary Artery Pressure). This center lumen is terminated proximally with a female luer-lock hub extension and is marked "PA DISTAL". Two custom, removable, user-formable stainless steel stylets (one straight, one curved) are also supplied with the ALERT® Catheter and are placed in the distal lumen to aid in steering the distal tip of the catheter into the left pulmonary arch.

Each custom stylet is coated with Teflon (registered trademark of Dupont, Inc.) to simplify insertion/withdrawal and terminates proximally with a male luer-lock orbicular knob.

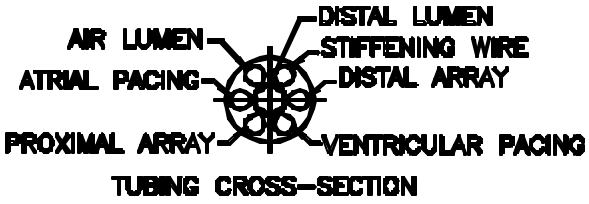


Fig. 3

The remaining six smaller lumens (Fig. 3) are used to embody the electrode conductor wires (atrial pacing/sensing, ventricular pacing/sensing, proximal right atrial defibrillation array lumen, distal left pulmonary artery defibrillation array lumen), a stiffening wire, and air lumen for balloon

inflation (See above cross section). The balloon inflation lumen terminates distally under an 8 mm x 13 mm (fully-inflated dimensions) natural latex balloon. The proximal end of this lumen connects to a balloon inflation extension marked "BALLOON INFLATION," which includes a two-way stopcock with female luer-lock hub.

B. ALERT® Companion

Fig. 4

The ALERT® Companion (Fig. 4) is a line-powered unit with battery backup and interfaces with the ALERT® Catheter to provide temporary transmission of R-wave synchronized, low-energy internal atrial defibrillation, intracardiac pacing and sensing, ECG recording, and pressure monitoring of the heart. The system is designed to delivery energy with biphasic pulses from 0.5 to 15 Joules in 0.5 Joule increments.

- Low-energy atrial cardioversion with R-wave synchronization
- Atrial and ventricular bradycardia pacing and sensing
- Hemodynamic pressure monitoring
- Catheter impedance measurement
- 12-Lead surface ECG input and printout

Defibrillation and pacing pulses are sent through the catheter as directed by the user through a user interface consisting of a keyboard and LCD display. The signals can be directed to a strip chart printer for archiving.

The safety features of the ALERT® Companion system include: diagnostic self tests with error messages; system self protection from external shocks; system disabling upon power up in the event of serious self test errors; error messages; identification of synchrony detection lead disconnect; patient isolation from power supply; protection from leakage current; EMI/RFI shielding; and low battery indicator.

C. ALERT® Interface Cable

The ALERT® Catheter (Fig. 5) is connected to the ALERT® Companion System via a proprietary ALERT® Interface Cable, which has a nominal length of 1.5 meters.

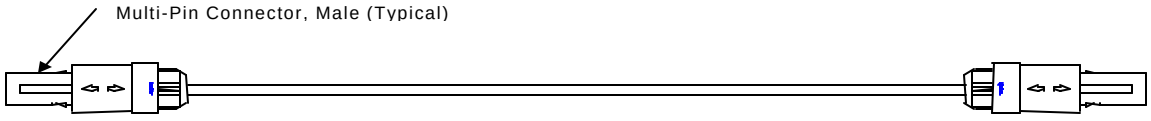


Fig. 5®

As a system, the product delivers up to 15 Joules, biphasic, individual pulses through two large area electrode arrays on the ALERT® Catheter, one located in the pulmonary artery and one located in the right atrium. Atrial sensing is provided from a small surface area electrode located on the catheter in the right atrium. The system also senses the endocardial ventricular ECG coming from a small surface area electrode on the ALERT® Catheter in the right ventricle in reference to the large area pulmonary artery electrode. In addition, the ALERT® System can be used as a complete single-chamber, atrial external pacemaker with typical constant current output. The system provides unipolar pacing and sensing from 2 small surface area electrodes on the catheter,

one in the right atrium and one in the right ventricle. The temporary pacemaker is programmable and operates in synchronous or asynchronous pacing modes with typical programmable parameters such as rate, current, sensitivity, etc.

The pacing and sensing electrodes on the ALERT® catheter are free floating (they are not always in contact with the heart wall). As a result, catheter movement and electrode placement are critical and will affect ventricular pacing and sensing functions and the ability to synchronize for shock delivery. The system was designed to avoid non-synchronized shocks. The ALERT® Companion is required to wait a maximum of 4 seconds for a minimum of 2 sensed ventricular beats prior to delivery of the atrial shock. If the ALERT® Companion is unable to detect at least 2 consecutive ventricular events during the 4-second window, the shock is aborted. The physician then has the option of checking or adjusting the catheter position before attempting to re-shock. Each time, the device checks for consistent sensing and synchronization so there is never any danger to the patient if the electrodes cannot detect a ventricular beat.

V. WARNINGS AND PRECAUTIONS

The warnings and precautions for the can be found in the ALERT® System labeling: ALERT® System Instruction Manual and the ALERT® Catheter Instructions for Use.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The alternative practices and procedures to the ALERT® System comprise of treatment with antiarrhythmic drugs (pharmacologic cardioversion) and/or the administration of external high energy shocks (direct current cardioversion).

VII. MARKETING HISTORY

The ALERT® system has been marketed in the following countries: United Kingdom, Italy, Czechoslovakia, United Arab Emirates, China (Hong Kong), Spain, Greece, Germany, Austria, France, Denmark, Holland, Hungary, Turkey and Russia. This device has not been withdrawn from the market in any country for any reason related to safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Reported Adverse Events

Adverse event rates and device comp lications are calculated as a percentage of the total number of treatment attempts for each group, namely the internal (study group) and the external (control group). This includes 156 randomized treatments (77 internal and 79 external), 34 crossover treatments (18 internal and 16 external), 3 patients who had an incomplete treatment (3 internal) and 3 patients who were treated twice (2 internal and 1 external).

Each adverse event was assigned a level of severity by the reporting institution. Severity was designated as mild, moderate, severe, and life threatening. There have been no deaths or *unanticipated* serious adverse events reported for either the ALERT® System device or the control device.

Adverse events were also stratified according to treatment group and relationship to the device (see Table 1). The manifestations of device-related adverse events from the control and study groups revealed some differences due to the nature of the treatment procedure itself (external vs. internal). The control group received atrial defibrillation therapy from an external device (standard transthoracic cardioversion approach), while the study group received treatment using an internal defibrillation catheter (transvenous procedure).

Forty-seven patients experienced first-degree skin burns, 10 patients developed skin rash, and 2 patients presented with post-procedure chest pain. One patient presented with a slow junctional rhythm after the procedure and was treated with medication. All of them were judged as either mild (50 reports) or moderate (10 reports).

Table 1. Adverse Events Reported for ALERT® Study

Device Related Event	External Device Related (n = 96)	ALERT® System Related (n = 100)
Abnormal Rhythm	1 (1%)	2 (2%)
Bleeding/Hematoma	0	3 (3%)
Bruising	0	4 (4%)
Ecchymosis of Catheter Site	0	1 (1%)
Hypotension	0	1(1%)
Infection/sepsis	0	1 (1%)
Pain, post-procedural	2 (2%)	0
Skin Burns	47 (49%)	0
Skin Rash	10 (10%)	0
Soreness at insertion site	0	1 (1%)
Ventricular Tachycardia	0	1 (1%)
Ventricular Fibrillation	0	1 (1%)
Other – hardening of the skin	0	1 (1%)
Other – swelling at insertion site	0	1 (1%)
Total	**60 (62%)**	**17 (17%)**

There were fewer patients who had adverse events related to internal cardioversion using the ALERT® Catheter and ALERT® Companion system. The types of device-related adverse events included ventricular fibrillation, ventricular tachycardia, abnormal rhythms, hypotension (due to a vagal response from the neck stick), infection/sepsis (near the left brachial vein), bruising, hematoma, swelling, soreness, ecchymosis and hardening of the skin, all which occurred at the site of catheter insertion.

The two patients who had abnormal rhythms following the procedure included one with a right bundle branch block that spontaneously resolved and the other with first degree AV block. Neither patient required intervention. In addition to the abnormal rhythms, the two patients undergoing internal cardioversion in which one patient presented with ventricular fibrillation, VF (life threatening) and the other patient presented with ventricular tachycardia, VT (severe) were caused by a malfunction of the ALERT® Companion during the ventricular threshold test. The level of severity for the internal treatment group were reported as life-threatening (1) severe (1), moderate (2), mild (13).

Two additional patients undergoing internal cardioversion experienced severe episodes of ventricular tachycardia several days after the internal procedure, both were judged unrelated to the treatment device.

Potential Adverse Events
Potential risks associated with either internal or external cardioversion listed alphabetically:

- Death
- Elevation of cardiac enzymes
- Hypotension
- Myocardial infarction
- Other abnormal rhythm (other than atrial fibrillation)
- Stroke
- Thromboembolism
- Ventricular fibrillation

- Ventricular Tachycardia

Potential risks uniquely associated with external cardioversion include and are listed alphabetically:

- Joint injury
- Post-procedural pain
- Residual muscular weakness or weakness
- Risks associated with general anesthesia
- Skin burns
- Skin rash

The potential risks associated with use of the ALERT® Catheter include those encountered with the introduction and placement of any temporary cardiac balloon catheter/pacing lead. Additional risks may be incurred as a result of the delivery of electrical energy during internal defibrillation and are listed alphabetically.

- Allergic reaction to latex balloon
- Balloon rupture resulting in air/latex embolus
- Bleeding, hematoma or thrombus at the catheter introduction site
- Bruising swelling, and/or irritation at the catheter introduction site
- Electrode displacement resulting in inappropriate or loss of sensing
- Electrode displacement resulting in loss of capture
- Infection/sepsis
- Intercostal or phrenic nerve stimulation
- Mechanical induction of arrhythmias or asystole
- Perforation causing cardiac tamponade with need for percutaneous or surgical drainage
- Perforation of the chamber or vessel wall
- Pneumothorax
- Pulmonary artery rupture or pulmonary hemorrhage
- Pulmonary infarction
- Tricuspid and/or pulmonic valve injury
- Vasospasm

The risks associated with use of the ALERT® Companion include those encountered with interfacing any electrical energy source via connecting cables to an intravascular catheter placed in direct contact with the heart. Additional risks may be incurred as a result of the delivery of electrical energy during internal atrial defibrillation.

- Inappropriate sensing of the R-wave resulting in the delivery of a mistimed electrical shock and the subsequent induction of VT or VF
- Loss of electrical output resulting in failure to pace/defibrillate
- Inappropriate electrical output resulting in induction of VT or VF
- Random aberrant behavior resulting in output settings different than those which are displayed or programmed

IX. SUMMARY OF PRE-CLINICAL STUDIES

Prior to initiating the clinical studies, testing was conducted in accordance with established national and international industry standards (See Table 2 below). Where no applicable standards exist, testing was conducted per EP MedSystems product specification and test requirements.

Biocompatibility Testing

Nonclinical laboratory studies were also conducted to determine the biocompatibility of the ALERT® Catheter. These biological tests (which included cytotoxicity, sensitization, pyrogenicity, hemolysis and other tests) exceeded the requirements of ISO-10993, Part 1 as modified by the FDA in memorandum (#G95-1). These tests were performed by NAmSA under contract and oversight by EP MedSystems. They were conducted in accordance with Part 58. Exceptions are addressed in the biological testing section of the ALERT® Catheter Design Validation Report, titled "Statement of cGLP for the ALERT® Catheter." The main deviation is in the substitution of a "study team" with oversight which was provided by EP MedSystems personnel working closely with NAmSA.

Table 2. Pre-Clinical Testing Summary

TEST (ALERT® Companion)	OBJECTIVE	SAMPLE SIZE	PASS/FAIL CRITERIA	TEST RESULTS
EMI Emissions Testing	To determine compliance with applicable electrical req'mts	1	EN 55011	Passed
EMI Immunity Testing	To determine compliance with the EMC Directive 89/336/EEC	1	EN60601-1-1	Passed
Software Verification/Validation Testing	To provide objective evidence that the design outputs meet all specified initial requirements	1	EPMED Document #33-0013-0000	Passed
Functional, Electrical, and Environmental	To determine acceptable compliance to design specification	1	EPMED Document #33-0013-0000	Passed
TEST (ALERT® Catheter)	**OBJECTIVE**	**SAMPLE SIZE**	**PASS/FAIL CRITERIA**	**TEST RESULTS**
Resistance / Electrical Conductivity Testing	To assess electrical resistance against product specifications	13	< 5 ohms Per original Product Specifications	Passed
Insulation Integrity Testing	To assess electrical leakage in the catheter body	13	<2.0 milliamps	Passed
In Vitro Atrial Defibrillation Pulse Testing	To test worst case electrical pulsing at max. voltage	13	Visual Inspection < 50% of original resistance	Passed
Interface Cable Connector Pin Connect / Disconnect Cycle	To test multiple connect/disconnect cycles w/o compromising conductivity	13	<10% increase of resistance from originally measured	Passed
Visual Inspection	To inspect acceptable workmanship levels	13	Per design validation #4027	Passed
Dimensional Inspection	To inspect various dimensional features	13	Ref: Ass'y Drawing #B74-0287	Passed
Joint Pull Testing	To test catheter joints	13	.55 lbs. axial load w/o functional damage	Passed
Flexural Testing	To test (simulate) flexural durability while indwelling in the heart	13	108,000 flex cycles w/ no loss in continuity/resistance	Passed
Thermal Shock Testing	To test catheters durability when subjected to thermal changes	13	Mil-std-202F, Method 107G	Passed
Balloon Inflation Media Leak Testing	To test integrity of balloon inflation	13	Balloon must be free of any air leaks	Passed
Balloon Burst Strength testing	To test /establish a safety margin for over-inflation of balloon	13	Must withstand 1.25 times the max. inflation	Passed
Balloon Inflation / Deflation Dwell Time / Cycle Fatigue Testing	Test durability of balloon when subjected to cyclic inflation fatigue	13	Must meet minimum 72 cycles without any balloon failures	Passed
Stylet Insertion / withdraw force testing	To test stylet insertion forces to be within acceptable limits	13	Withdraw force to be < 1.0 pounds	Passed
Distal Lumen Natural Frequency HZ Testing	To test/measure resonant frequency	13	Must exhibit resonant frequency capable of measuring CVP, PCWP, MPAP	Passed
Shelf-Life Testing	To determine shelf-life of device	13	Must pass sterility and functional test	Passed
Sterilization Testing	To determine sterility of device	10	Sterilization Validation	Passed
Biocompatibility Testing *	To test the biocompatibility of the ALERT® Catheter		ISO-10993-1, FDA Guidance #G95-1	Passed

X. SUMMARY OF CLINICAL STUDY

Between October 1997 and August 2000, EP MedSystems, Inc. conducted a clinical study to determine the safety and effectiveness of the ALERT® Companion defibrillation system for its ability to convert atrial fibrillation. The study was not designed to evaluate other arrhythmias or rapid atrial pacing.

A. Objective

The primary objective of the ALERT® clinical study was to determine whether the probability of successful termination of atrial fibrillation with the ALERT® System (an internal defibrillation system) is equivalent to that of cardioversion using an external defibrillator using patches in the AP (anterior-posterior) orientation. Atrial fibrillation (AF) is defined from the electrocardiogram as a narrow QRS complex without P waves or flutter waves and with an irregular ventricular response. The study endpoint for device effectiveness is the proportion of randomized patients who have their AF terminated by the intervention strategy.

Successful acute defibrillation was defined as:

- The resultant intrinsic rhythm must be a sinus rhythm, atrial rhythm (less than 100 beats per minute), junctional rhythm, or paced rhythm without underlying atrial fibrillation, atrial flutter, or atrial tachycardia.
- The resultant intrinsic rhythm must be manifest on ECG within 30 seconds of the shock.
- The resultant intrinsic rhythm must not revert to AF for a period of at least 5 seconds.

In addition to delivering shocks for atrial defibrillation, effectiveness of the ALERT® System also evaluated the device's ability to correctly sense and pace the right ventricle, correctly sense the atrium, and R-wave synchronization.

Safety was evaluated by quantifying the incidence of adverse events associated with the intervention strategies and the incidence of device complications associated with the intervention strategies.

B. Study Design

A prospective, non-blinded, randomized, multicenter trial involving 12 investigational centers evaluated the safety and effectiveness of the ALERT® System with patients who are candidates for the treatment of atrial fibrillation by cardioversion. All patients (adults) enrolled in the study were randomized to either internal (new treatment) or external cardioversion (control intervention). For the purposes of the 'intention-to-treat' analysis, only 156 of the 162 treatment attempts are valid for assessing effectiveness. Assessment of safety was performed on 162 treatment attempts.

Statistical analysis was performed using a statistical analysis package, SAS. Baseline characteristics were compared between treatment groups and investigational sites using a chi-square test statistic for 2 x 2 contingency tables. Fisher's exact test was used when expected cell frequencies were <5. The Cochran-Mantel-Haenzel (CMH) test statistic for general association was used when the number of levels for each row variable was greater than 2. Baseline characteristics were also tested for association with the treatment outcome. The chi-square and CMH test for general association were used to determine the significance of each variable and relative risk ratios were calculated for those variables that resulted in a

significant p-value. Quantitative variables were compared for each treatment outcome using a 2-sample t-test. All tests of significance were two-tailed and conducted at an alpha level of 5%, and p-values, which were 0.05 or less, were considered to be statistically significant.

C. **Patient Demographics**

A total of 156 patients, 44 females and 112 males were included in the study. Patients ranged in age from 25 to 89 years with a mean age of 61 years. Patient characteristics for each treatment group are presented in Table 3 below.

Table 3. Characteristic of Patients with AF Undergoing Internal and External Cardioversion (n = 156)

Characteristic	**External n (%)** mean ± SD	**Internal n (%)** mean ± SD	**Significance**
Number of patients	79	77	**NS**
Age	61 ± 12	61 ± 11	**NS**
Male (Female)	57 (22)	55 (22)	**NS**
Body Mass Index	34 ± 9	33 ± 11	**NS**
BMI => 25	67 (85%)	63 (82%)	**NS**
Left Atrial Size (mm)	45 ± 6.6	46 ± 5.7	**NS**
LAD>4.5 cm	43 (54%)	40 (52%)	**NS**
Left Ventricular Ejection Fraction	47 ± 13	51 ± 12	**NS**
LVEF<40%	21 (27%)	13 (17%)	**NS**
Concomitant Heart Disease	47 (59%)	49 (64%)	**NS**
Failed Prior External Cardioversion	49 (62%)	50 (65%)	**NS**
Failed Prior Drug Therapy	69 (87%)	62 (81%)	**NS**
Cardiac Surgery	12 (15%)	11 (14%)	**NS**
Pacemaker/ICD	4 (5%)	5 (6%)	**NS**
Duration of AF (months)	8.7 ± 13	8.5 ± 16	**NS**
Duration AF > 6 months	24 (30%)	22 (29%)	**NS**

D. **Gender Bias Analysis**

With a total of 156 patients, 44 females and 112 males were included in the study. The ratio of males to females was approximately 3:1 for the study group. This ratio is considered typical of the atrial fibrillation patient population found in the literature. The selection of patients was biased on the basis of gender. However, there were no differences of safety and effectiveness of the device based on gender.

E. **Study Results**

Primary external defibrillation was performed in 79 patients using patch defibrillation electrodes and primary internal defibrillation was performed in 77 patients using the ALERT â System. In addition, internal defibrillation was performed as a crossover procedure in 18 patients who failed to convert with external defibrillation. External defibrillation was performed as a crossover procedure in 16 patients who failed to convert with internal defibrillation. In total, 95 patients underwent internal defibrillation and 95 patients underwent external defibrillation including randomized and crossover procedures.

Analysis of Site Interaction

The influence of investigational site interaction on primary success for randomized and crossover procedures combined (n=190) is presented in Table 4 below. The proportion of successful outcomes was calculated separately for each site. The probability value for site interaction (chi-square and CMH) was provided separately for each treatment group and represents differences between sites within that group. The majority of sites reported a success rate of 70% or higher for each of the treatment groups. However, three sites reported success rates below 50% which results in a chi-square and CMH probability value < 0.05.

Table 4. Primary Success Rates by Investigational Site for Randomized and Crossover Treatments Combined (n = 190)

Site	Internal Success % (n)	External Success % (n)
Chi-Square	0.003	0.03
CMH	0.003	0.03
01	70% (7/10)	50% (5/10)
02	100% (11/11)	86% (6/7)
03	86% (6/7)	50% (3/6)
04	95% (20/21)	79% (15/19)
05	40% (4/10)	20% (2/10)
06	25% (1/4)	60% (3/5)
07	75% (3/4)	80% (4/5)
09	0% (0/2)	33% (1/3)
10	75% (9/12)	88% (15/17)
11	100% (3/3)	100% (3/3)
12	71% (5/7)	71% (5/7)
13	75% (3/4)	67% (2/3)

Effectiveness Results

The primary success rate for the internal defibrillation procedure (randomized + combined) was 76% (72 of 95 patients successfully converted) compared with a success rate of 67% for the external defibrillation procedures (64 of 95 patients successfully converted). At one hour post-treatment, the combined secondary success rate for internal defibrillation was 72% (68/95) compared to 58% (55/95) for external defibrillation. After 4 weeks of follow-up, 42 out of 68 (62%) of the combined patients treated with internal defibrillation were still in sinus rhythm compared to 29 out of 55 (53%) of the patients treated with external defibrillation. Table 5 below provides the proportion of successful outcomes for each treatment group and the 95% confidence interval for the observed difference between of the two groups including the 95% confidence interval on the success rates themselves. Only those patients valid for assessing effectiveness were included in this table (n=156).

Table 5. Proportion of Success for Randomized and Combined Treatments

Treatment	Primary Success Rate (5 Seconds)		Difference	95% C.I.	95% C.I. on Success Rate	
Randomized (n = 156)	**Internal**	79% (61/77)	4%	-10% to 21%	**Internal**	68% to 88%
	External	75% (59/79)			**External**	64% to 84%
Combined (n = 190)	**Internal**	76% (72/95)	9%	-6% to 23%	**Internal**	66% to 84%
	External	67% (64/95)			**External**	57% to 77%
	4-Week Success Rate (4 Weeks)			**95% C.I.**	**95% C.I. on Success Rate**	
Randomized (n = 156)	**Internal**	61% (35/57)	13%	-6% to 34%	**Internal**	48% to 74%
	External	48% (24/50)			**External**	34% to 62%
Combined (n = 190)	**Internal**	62% (42/68)	9%	-6% to 24%	**Internal**	49% to 73%
	External	53% (29/55)			**External**	44% to 62%

Ventricular pacing thresholds were recorded for 82 out of 95 (86%) patients and ventricular sensing thresholds were recorded for 94 out of 95 (99%) patients. The mean ventricular pacing threshold was 12.1 mA +/- 7.2 and the mean ventricular sensing threshold was 2.4 mV +/- 2.0. Both of these parameters were considered within the normal expected range for pacing and sensing in the ventricle indicating proper function of these effectiveness parameters. Ventricular sensing was rated consistent for 89% of the patients tested (84/94). Ten patients (11%) exhibited intermittent sensing. However, the lack of consistent sensing did not interfere with the device's ability to shock safely.

There were no reported failures to deliver R-wave synchronized shocks. A total of 345 shocks were delivered during the clinical study and there were no reported incidents of inappropriate shock delivery. The internal treatment group (n = 95) received a total of 345 shocks with a mean energy of 7.6 ± 3.9 joules delivered for each patient. For the patients who were successfully cardioverted (72/95), the mean energy delivered to each patient was 9.7 ± 3.2 joules (randomized and crossover treatments combined). The mean energy required for the internal crossover group (n = 18) was 10.6 +/- 3.1 joules and for the randomized group (n = 61) was 9.5 +/- 3.2 joules. On average, patients having a successful outcome with the ALERT® System received 3.2 +/-1 shocks. The median number of shocks required for success was 3. Impedance measurement values ranged from 13 to 145 ohms with a mean impedance of 53 +/- 12 ohms.

Atrial sensing thresholds were reported on 58 of the 72 patients in sinus rhythm. Excluding one outlying value (20mV), the mean atrial-sensing threshold for the remaining 57 patients was 1.5 +/- 1.9 mV with a range of 0.1 to 10.0 mV. This is consistent with normal atrial sensing thresholds indicating proper sensing function of the device. At one-half the measured threshold, atrial sensing was rated consistent for 74% (43/58) of the patients tested. Nine (16%) patients exhibited intermittent sensing and 6 patients (10%) exhibited complete failure to sense. Atrial pacing was not tested in any of the subjects.

Safety results

There were no deaths or unanticipated adverse events associated with either internal or external cardioversion. There was one incidence of VF that required an external rescue shock in the internal treatment group. Another patient had VT. Both were attributed to device malfunction of the ALERT® Companion. The ALERT® Companion aborted delivery of defibrillation shock. A software error caused the device to incorrectly sense the rate of the incoming ventricular signal

that is used for R-wave synchronization, which caused the device to abort shock delivery. Although the sensing problem was due to a software error, the upper rate limit was triggered appropriately and the device functioned as designed. The software error was resolved in a subsequent revision level. Two patients experience abnormal heart rhythms that did not require intervention. Two out of 95 patients in the internal treatment group required back up ventricular pacing after cardioversion. The device is also designed with an algorithm that will avoid non-synchronized atrial shocks (see discussion in the Device Description section).

Thirteen adverse events associated with catheter placement included bruising, hematoma, swelling, soreness, ecchymosis, hardening of the skin, hypotension and infection. The majority of adverse events were associated with pads (external electrodes) placement and higher energy cardioversion from the external defibrillator. They included 47 skin burns and 10 skin rashes. Two patients complained of post-procedural chest pain.

XI. CONCLUSIONS DRAWN FROM STUDIES

Pre-clinical studies performed on the ALERT® System (ALERT® Companion™ with Software version V1.08, ALERT® Catheter, and ALERT® Interface Cable) demonstrated that the system is adequate for its intended use. The subsequent clinical study determined its ability to convert atrial fibrillation. The results of in-vitro and in-vivo studies provided reasonable assurance that the ALERT® System (ALERT® Companion™ with Software version V1.08, ALERT® Catheter, and ALERT® Interface Cable) is safe and effective when used as indicated in the labeling.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the FDA has the clinical expertise to address the clinical issues for this device. The risks to health in internal defibrillation are clearly characterized and well known in the medical community and by FDA.

XIII. CDRH DECISION

The ALERT® System was granted expedited review status, because the device allows lower atrial defibrillation thresholds and therefore, may offer a viable alternative to higher energy external electrical cardioversion/defibrillation in some patients with atrial arrhythmias.

The applicant's manufacturing and sterilization facilities were inspected and found to be in compliance with the device Quality System Regulation (21 CFR 820). CDRH issued an approval order on November 27, 2002.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.